were inserted to more clearly define the present invention. Support for these amendments is found at page 3, line 30 through page 4, line 5, and page 14, lines 27-33 of the Substitute Specification filed September 17, 2001.

The foregoing amendments are made without any intention to abandon the subject matter of the claims as filed, but with the intention that claims of the same, lesser or greater scope may be pursued in the present application or in a continuation, continuation-in-part or divisional application. Applicants believe that the present amendment does not add new matter. No new matter has been added by the present amendments.

Improper Markush

The Examiner states that: "The claims are improperly set forth as the genus claims [which] encompass multiple distinct peptides, as identified and claimed, which fail to share the characteristics of a genus, i.e., a common utility and a substantial structural feature essential to the disclosed utility." February 13, 2002 Restriction Requirement at page 2. The Examiner further states that, alternatively, the claims define multiple structurally distinct compounds capable of different use, with different modes of operation, different function and different effects. The Examiner states that a reference against one of the claimed components or methods would not be a reference against the other.

Although the Office Action does not recite which claims present the alleged improper Markush group, Applicants assume that the Examiner is referring to claims 46 and 69, which lists a series of amyloid proteins which can be used in the methods of the present invention. Applicants respectfully submit that the Specification provides a common utility and a substantial structural feature essential to the disclosed utility for these amyloid proteins. As described at page 2, lines 13-20 of the Substitute Specification:

> Each amyloidogenic protein has the ability to organize into β-sheets and to form insoluble fibrils which get deposited extracellularly or intracellularly. Each amyloidogenic protein, although different in amino acid sequence, has the same property of forming fibrils and binding to other elements such as proteoglycan, amyloid P and complement component. Moreover, each amyloidogenic protein has amino acid sequences which, although different, will show similarities such as regions with the ability to bind to the glycosaminoglycan (GAG) portion of proteoglycan (referred to as the GAG binding site) as well as other regions which will promote β-sheet formation.

The Specification futher teaches that all-D peptides can be used as vaccines and trigger an immune response. See, for example, page 7, lines 23-28 and page 12, lines 32-34 of the Substitute Specification. However, in order to expedite prosecution of the present application, Applicants have amended the claims to amyloid-β (Aβ) peptides and withdrawn claims 55 and 69, which had the Markush group. Accordingly, Applicants respectfully require reconsideration and withdrawal of this objection.

Restriction Requirement

The Examiner has required restriction to one of the following inventions under 35 U.S.C. 121:

I. Claims 46-69 and 93-98 in part drawn to distinct methods of treating and/or preventing with a peptide, classified for example in class 514, subclass 2.

II. Claims 70-92 and 99-103 in part drawn respective to distinct compositions, classified for example in class 530, subclass 350.

Applicants provisionally elect the invention of Group I, drawn in part to distinct methods of treating and/or preventing with a peptide, classified for example in class 514, subclass 2 and reserve the right to prosecute the non-elected claims in a continuing application.

The Examiner has required further restriction under 35 U.S.C. 121 to one of the following peptides: (1) C-terminal region' (2) β-sheet region; (3) GAG-binding site region; (4) cellular adherence region; (5-67) peptides corresponding to SEQ ID NO: 1-63; peptides of (68) Aβ(1-42); (69) beta sheet region of IAPP; (70) β_2-microglobulin; (71) amyloid A protein, (72) a prion-related protein; and (73) macrophage adherence region.

Applicants provisionally elect SEQ ID NO:27, with traverse. As described above, Applicants have withdrawn claims 55 and 69 with the Markush group to different amyloid proteins, including Aβ(1-42), beta sheet region of IAPP, β2-microglobulin, amyloid A protein, and prion-related proteins. In addition, independent claims 46 and 56 have been amended to all-D amyloid-β (Aβ) peptides. Accordingly, as illustrated in FIG. 1 of the Specification, the

remaining peptides are various fragments of Aβ(1-42) that can be used in the methods of the present invention and represent various species under a genus.

A restriction is proper only if the inventions are "**independent and distinct.**" The MPEP §802.01 defines independent as follows:

> The term "independent" (*i.e.*, not dependent) means that there is no disclosed relationship between the two or more subjects disclosed, that is, they are unconnected in design, operation or effect, for example, (1) species under a genus which species are not usable together as disclosed or (2) process and apparatus incapable of being used in practicing the process.

The peptides in the claimed method of the present invention are, in fact, members of the same superfamily of all-D Aβ peptides that induce an immune response to at least one region of the Aβ peptide. Accordingly, since the described all-D peptides (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility, Applicants respectfully submit that unity of invention exists for the all-D peptides included within the Markush group of the claims of the present application, and request withdrawal of this election requirement.

Election of Species

Applicants provisionally elect the following species:

From Species 1): selected from R' or N-terminal substituents of: A) hydrogen;

From Species 2) selected from R" or C-terminal substituents of: E) unsubstituted amino groups;

From Species 3) disease: M) Alzheimer's

All the claims in the elected group are readable on the elected species. However, Applicants request modification of the present election requirement under 37 C.F.R. §1.143. According to M.P.E.P. § 803.02:

> If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, **the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions.** In such a case, the examiner will not follow

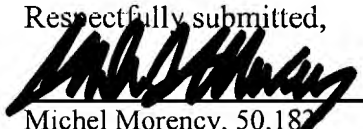
> the procedure described below and will not require restriction. Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), **it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention**. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). **Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility**.

The peptides in the claimed method of the present invention are, in fact, members of the same superfamily of all-D Aβ peptides that induce an immune response to at least one region of the Aβ peptide. Accordingly, since the described all-D peptides (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility, Applicants respectfully submit that unity of invention exists for the all-D peptides included within the Markush group of the claims of the present application, and request withdrawal of this election requirement.

CONCLUSION

On the basis of the foregoing remarks, Applicants respectfully request the withdrawal or modification of the present election requirement under 37 C.F.R. §1.143. Further, in view of the above arguments and comments, Applicants respectfully submit that the present case is in condition for allowance, and as such a Notice of Allowance is respectfully requested. Should there be any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

At page 11, please delete lines 16-18 and insert:

--SEQ ID NO: 25 Lys-Leu-Val-Phe-Phe-Ala-[Gln]Glu (all-D)

SEQ ID NO: 26 Lys-Leu-Val-Phe-Phe-Ala-[Gln]Glu-NH_2 (all-D)

SEQ ID NO: 27 His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-[Gln]Glu (all-D)--

In the Claims:

Claims 57 and 65 have been canceled.

Please amend claims 46-48, 50-52, 54, 56, 59-62, 64 and 67 as follows:

46. (Amended) A method for preventing and/or treating an amyloid-related disease in a subject, comprising: administering to the subject an antigenic amount of an all-D amyloid-β peptide, wherein said all-D amyloid-β peptide [elicits the production of antibodies against said all-D peptide and] induces an immune response by said subject against said amyloid-β peptide [, thereby preventing and/or reducing amyloid-induced amyloid fibril formation or neurodegeneration].

47. (Amended) The method of claim 46, wherein said all-D amyloid-β peptide interacts with at least one region of an amyloid protein, said region being selected from the group consisting of: C-terminal region, β sheet region, GAG-binding site region, cellular adherence region, immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof.

48. (Amended) The method of claim 46, wherein said all-D amyloid-β peptide further comprises:

an N-terminal substituent selected from the group consisting of:

hydrogen;

lower alkyl group consisting of acyclic or cyclic having 1 to 8 carbon atoms;

aromatic group;

heterocyclic group; and

acyl group; and

a C-terminal substituent selected from the group consisting of hydroxy, alkoxy, aryloxy, unsubstituted and substituted amino groups.

50. (Amended) The method of claim 48, wherein said all-D amyloid-β peptide further comprises an acid functional group, or a pharmaceutically acceptable salt or ester form thereof.

51. (Amended) The method of claim 48, wherein said all-D amyloid-β peptide is selected from the group consisting of SEQ ID NOS: 1-48.

52. (Amended) The method of claim 51, wherein said all-D amyloid-β peptide is modified by substituting at least one amino acid residue with another amino acid or non-amino acid fragment.

54. (Amended) The method of claim 51, wherein said all-D amyloid-β peptide is modified by removing or inserting at least one amino acid residue.

56. (Amended) A method for preventing and/or treating an amyloid-related disease in a subject, comprising administering to the subject an antigenic amount of a peptide having Formula I:

$$R'—(P)—R'' \qquad (I)$$

wherein

P is an all-D amyloid-β peptide [of a fibril or amyloid protein] selected from the group consisting of: Aβ(1-42, all-D), C-terminal region, β sheet region, GAG-binding site region, cellular adherence region, immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof;

R' is an N-terminal substituent selected from the group consisting of:
hydrogen;
lower alkyl group consisting of acyclic or cyclic having 1 to 8 carbon atoms;
aromatic group;
heterocyclic group; and
acyl group; and

R" is a C-terminal substituent selected from the group consisting of hydroxy group, alkoxy group, aryloxy group, unsubstituted group, and substituted amino group,

wherein said all-D amyloid-β peptide induces an immune response by said subject against said all-D amyloid-β peptide.

57. Canceled

59. (Amended) The method of claim 56, wherein said all-D amyloid-β peptide further comprises an acid functional group, or a pharmaceutically acceptable salt or ester form thereof.

60. (Amended) The method of claim 56, wherein said all-D amyloid-β peptide further comprises a base functional group, or pharmaceutically acceptable salt form thereof.

61. (Amended) The method of claim 56, wherein said all-D amyloid-β peptide is selected from the group consisting of SEQ ID NOS: 1-48.

62. (Amended) The method of claim 61, wherein said all-D amyloid-β peptide is modified

by substituting one or more amino acid residues with other amino acid or non-amino acid fragment.

64. (Amended) The method of claim 61, wherein said all-D amyloid-β peptide is modified by removing or inserting one or more amino acid residues.

67. (Amended) The method of claim 56, wherein said disease is cerebral amyloid angiopathy [(CAA)].

Please add the following new claims:

104. (New) The method of claim 46, wherein said immune response prevents and/or reduces amyloid fibril formation.

105. (New) The method of claim 46, wherein said immune response prevents and/or reduces amyloid-induced neurodegeneration.

106. (New) The method of claim 46, wherein said immune response prevents and/or reduces amyloid-induced cellular toxicity.

107. (New) The method of claim 56, wherein said immune response prevents and/or reduces amyloid fibril formation.

108. (New) The method of claim 56, wherein said immune response prevents and/or reduces amyloid-induced neurodegeneration.

109. (New) The method of claim 56, wherein said immune response prevents and/or reduces amyloid-induced cellular toxicity.